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### Differential Trajectories in Altered Insulin Sensitivity Following Weight Loss and Their Impact on Circulatory Amino Acids: Results from the PREVIEW: New Zealand Sub-study (OR27-07-19)

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**Objectives:** Metabolite profiling studies have consistently identified altered circulatory concentrations of amino acids (AAs) in individuals with heightened risk of type 2 diabetes and cardiovascular diseases. Of the changes reported to date, the branched-chain amino acids (BCAA) may be a reliable biomarker of disease risk and have been reported to be elevated many years prior to the onset of diabetes. We hypothesised that energy restriction-associated weight loss in pre-diabetes individuals would result in altered profile of circulatory AAs, including BCAA, with the changes correlating with the improvement in insulin sensitivity.

**Methods:** Pre-diabetic individuals (confirmed using the American Diabetes Association criteria) aged 25–70 years with BMI > 25 kg/m<sup>2</sup> recruited into the New Zealand arm of the PREVIEW diabetes prevention trial, participated in an 8-week weight reduction program, with a requirement to lose ≥ 8% initial body weight using a commercial

low-calorie diet (LCD, Cambridge Diet, UK<sup>TM</sup>). Among those who succeeded, current analysis based on available samples ( $n = 168$ ) from baseline (week-0) and end of weight loss (week-8). Serum free AA concentrations measured by ultra-high pressure liquid chromatography (UPLC) and all other metabolites measured using standard assays.

**Results:** Significant weight loss ( $11.1 \pm 0.2\%$  from baseline) accompanied improved insulin sensitivity and lipid profile. BCAA concentration positively correlated with insulin resistance measured at week 0 and 8, correspondingly ( $P < 0.05$ ). Although the concentration of some AAs reduced significantly from week 0 to 8 ( $P < 0.05$ ), reduction in fasting BCAA concentration was not significant ( $P > 0.05$ ). However, regression analysis demonstrated that independent of weight loss, every 1.0 standard deviation (SD) reduction in BCAA concentration was associated with improvement in insulin sensitivity by 1.9 SD ( $P < 0.05$ ).

**Conclusions:** As expected, dietary energy restriction-associated weight loss in individuals with pre-diabetes contributes towards normalisation of insulin sensitivity. Further, the responsiveness of AA and BCAA profiles to weight loss may be beneficial for monitoring and overseeing disease risk and improvement.

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